1100-41 An Angiographic Risk Score Integrating Both Epicardial and Tissue Level Perfusion Before and After Facilitated Percutaneous Coronary Intervention in Acute MI

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Background: Both epicardial and tissue level perfusion have been related to clinical outcomes in the setting of acute myocardial infarction (AMI), and the performance of adjunctive/rescue percutaneous intervention may alter clinical outcomes after thrombolytic administration. ***Objectives & Methods:*** The goal of this study was to develop a simple, broadly applicable method that integrates epicardial and tissue level perfusion both before and after PCI to arrive at a single angiographic risk score (ARS) in patients undergoing PCI after thrombolysis. The angiographic risk score is the arithmetic sum of the TIMI Flow Grade (0-3) added to the TIMI Myocardial Perfusion Grade (0-3) before and after PCI (total possible score of 0-12). This risk score was evaluated in patients from the LIMIT AMI trial of tPA monotherapy vs tPA plus rhuMAb CD18. Infarct size was assessed using 120-216 hr post-AMI SPECT Technetium-99m Sestamibi data. ***Results:*** Those patients with an angiographic risk score in the lowest group (0-6) had a risk of 30 day death or MI of 9.3% (5/54), whereas those with an ARS of 7-12 had a risk of 1.3% (1/79)(p=0.04). There were no deaths or recurrent MIs among patients with a risk score greater than 10. Likewise, larger SPECT infarct sizes were observed among patients with an ARS of 0-6 (22.6% ± 20.4%, n=53) compared to those patients with an ARS of 7-12 (12.3% ± 14.3%, n=71, p=0.001). In a second analysis, data from patients who did not undergo PCI was incorporated by using the final TIMI Flow Grade and the final TIMI Myocardial Perfusion Grade on diagnostic arteriography instead of the post PCI values, and similar results were seen: the risk of 30 day death or MI was 11.7% (11/94) for ARS of 0-6, whereas it was 4.2% (6/143) for ARS of 7-12. SPECT infarct sizes were larger for ARS of 0-6 (21.0 + 19.0, n=84) vs ARS of 7-12 (11.8 + 15.2, n=127, p=0.0001). ***Conclusions:*** The angiographic risk score integrates indexes of epicardial and tissue level perfusion before and after PCI or at the end of diagnostic cardiac catheterization to arrive at a single risk estimate that is associated with infarct size and 30 day death or MI. Failure to achieve an ARS of > 6 is associated with a doubling of infarct size.

1100-42 Myocardial Perfusion in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome Assessed With Venous Contrast Echocardiography

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Non ST segment elevation acute coronary syndrome (NSTEACS) is a dynamic condition and the underlying pathophysiology is currently thought to comprise not only atherosclerotic plaque rupture and superimposed thrombosis of an epicardial coronary artery but also microvascular obstruction to flow due to vasoconstriction, microembolisation and adherence of activated blood cells to microvascular endothelium. We therefore sought to compare venous myocardial contrast echocardiography (VMCE), a new bedside technique allowing for exclusive imaging myocardial vasculature, to Sestamibi SPECT (SI), angiographic and biochemical findings in patients with NSTEACS.

60 patients (women, n=15, age 65±11y) with typical anginal chest pain at rest or during minimal physical activity plus either transient EKG changes (without ST segment elevation) or elevated Troponin T (> 0.03 µg/ml) on presentation were included in the study. All patients underwent VMCE (3ml Optison in 27ml NaCl, 200ml/h, intermittent harmonic imaging every 5th endsystole, off-line digital image processing), SI and coronary angiography within 1 hour after presentation. 52/60 patients (87%) had myocardial contrast defects on VMCE. Concordance with respect to presence of myocardial defects on SI was 88% (k=0.74). 26/60 patients (43%) had TIMI flow <3; all of these patients had a contrast defect on VMCE and 17/26 patients (65%) had elevated Troponin I. 34/60 patients (57%) had TIMI flow 3; 26/34 patients (76%) had a contrast defect on VMCE and 14/34 patients (41%) had elevated Troponin I.

We conclude that VMCE is a promising method for evaluation of myocardial perfusion in patients with NSTEACS. It is reasonable to further investigate its role for diagnostic workup and follow up of patients with NSTEACS.

1100-43 Significant Myocardial Salvage in Patients With Non-ST Elevation Myocardial Infarction Is Common: Results Using Serial Myocardial Perfusion Imaging

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Background: Technetium-99m sestamibi can delineate both myocardium at risk and final infarct size in patient (pts) with myocardial infarction (MI). Serial myocardial perfusion imaging (MPI) in pts with non-ST elevation MI has not been described previously. **Methods:** Pts with non-ST elevation MI who had MPI at the time of Emergency Department (ED) presentation were included. Percent defect size was quantitated using a 50% threshold derived from a phantom (r=0.99) using multiple short axis slices. Myocardial risk area was defined as the initial defect size; infarct area as the defect size on repeat MPI; and myocardial salvage as the difference between the two. Ejection fraction (EF) was calculated using a previously validated computer algorithm (QGS). **Results:** There were 69 pts who had acute ED MPI and MI who underwent repeat MPI a median 5 days later. Revascularization was performed in 46 pts (67%) (only 2 within 12 hours of presentation). Variation in both mean peak CK (704±1223 U/L, median 377 U/L, range 91 to 9319 U/L) and risk area (19±10%, median 19%, range 2-46%) was high. Mean final infarct size, 11±+9% (median 9%, range 0-35%), was significantly smaller (p<0.001), and was only 57% of the initial risk area. Significant salvage (initial risk area-final infarct size >25%) occurred in most pts (67%), with 54% of pts having > 50% salvage. Pts with significant salvage had an increase in EF (48 to 55%, 22% increase, p<0.01), while those without significant salvage EF decreased (49 to 48%, 2% decrease, p=NS). **Conclusions:** The ischemic risk area in pts with non-ST elevation MI can be large. Significant myocardial salvage is common, is not limited to those that have early revascularization, and is associated with improved EF.

1100-44 Old Age and Myocardial Infarct Size in the Reperfusion Era

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It is well established that cardiac death and complications are more common in elderly patients who suffer myocardial infarction. Although the mechanism for this increased morbidity and morality is unknown, one potential explanation, extrapolated from some experimental models of myocardial ischemia/reperfusion, is that an age-associated increase in infarct size may play a role. Data on infract size in old versus young patients are lacking. We examined whether CK-MB determined myocardial infarct size differed in elderly (65 years or older) versus younger (< 65 years old) patients who did not have coronary reperfusion (from the prethrombolytic era MILIS study) and from the more recent thrombolytic TIMI 4 trial. Infarct size data in MILIS (MB infarct size index = area under MB-CK curve adjusted for body surface area) was collected in 639 patients < 65 and 213 elderly patients. Mean MB infarct size index was 15.59 ± 0.59 Units for those < 65 and 11.89 ± 0.83 Units for elderly patients (p = 0.0003). Infarct size data in TIMI 4 (MB-CK = average MB-CK over first 14 hours) was collected in 260 patients < 65 and 140 elderly patients. Mean MB-CK infarct size was 123.2 ± 8.3 International Units per liter (IU/L) in patients < 65 and 119.5 ± 10.4 IU/L for elderly patients (p = 0.78). The smaller infarcts in older MILIS patients were not due to lower presenting heart rates which were 79.8 beats/min (mean) in elderly patients and 80.4 for younger patients (p = NS); mean heart rates in TIMI 4 were 73.4 in elderly patient and 71.1 in younger patients (p = NS). These data suggest that in the absence of reperfusion, infract size is smaller (rather than larger) in older patients. Reperfusion changes this relationship resulting in equally sized infarcts in old versus young, suggesting that in the reperfusion era, infarct size is not larger in elderly patients and probably does not contribute to their worse outcome.

1100-45 Rarity of Circumflex Culprits in ST-Elevation MI is Due to Relative ECG Silence

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Background: Angiographic studies of ST-elevation myocardial infarction (MI) consistently document that the left circumflex coronary artery (CFX) is uncommonly the culprit vessel compared to the left anterior descending (LAD) and the right coronary (RCA). Since there is no a priori reason to expect a differential propensity of the three coronary vessels to acute plaque instability, we hypothesized that this disparity of CFX culprits may result from ECG insensitivity in detection of lateral wall transmural ischemia. If this hypothesis is correct, the distribution of culprit vessels in non ST-elevation acute coronary syndromes(ACS) would be expected to be relatively even. **Methods:** We retrospectively analyzed angiograms from our cath lab database to identify the culprit vessel in 166 pts with ST-elevation MI and in 134 others with non-ST elevation ACS. **Results:** In pts with ST-elevation MI, the CFX was uncommonly the culprit vessel (12%), compared to LAD (43%) or RCA (45%) involvement (CFX vs LAD or RCA, p<0.001). However, in pts with non-ST elevation ACS, the distribution of culprit vessels was more even and in fact the CFX was most frequently the culprit vessel (40%), whereas the LAD was responsible in 28% of pts and the RCA in 32% of cases (CFX vs LAD or RCA, p=NS). Compared to pts with ST-elevation, in those with non-ST elevation ACS the CFX was more commonly the culprit vessel (40 vs 12%, p<0.001). The frequency of LAD and RCA culprits was similar between the two groups. **Conclusions:** These findings document a striking disparity in the prevalence of CFX culprits in pts with ST-elevation MI compared to non-ST elevation ACS. The rarity of CFX culprits in ST-elevation MI but even distribution in other ACS, suggests that the CFX is just as likely to develop plaque rupture but that lateral wall transmural ischemia is often missed by ECG.

1100-46 Does Prior Angina Predict Outcomes Following Acute Myocardial Infarction? Testing the Relevance of Ischemic Pre-Conditioning in the Era of Primary Angioplasty

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Background: In animal studies, brief periods of myocardial ischemia reduce the size of the infarct resulting from a subsequent total occlusion. It is postulated that angina preceding acute myocardial infarction (AMI) may provide similar benefit in humans. However, clinical studies on the prognostic impact of preinfarction angina have shown mixed results.

Methods: We tested the effect of prior angina on in-hospital outcomes [ischemic target vessel revascularization (TVR), reinfarction, death, & MACE (combined end-point)] in the pooled database of 2558 patients enrolled in Primary Angioplasty in Myocardial Infarction (PAMI)-2 & Stent PAMI trials. To minimize confounding from silent ischemia & atherosclerotic burden, we excluded 878 (34%) patients with a history of diabetes, prior myocardial infarction, prior percutaneous coronary intervention or coronary artery bypass surgery from this analysis. In the remaining 1680 patients, we compared angiographic & clinical outcomes between patients with (n=230, 17%) & those without prior angina (n=1450, 83%).

Results: Prior angina patients had a higher incidence of hypertension (50 vs 40%), dyslipidemia (45 vs 33%), peripheral vascular disease (5.7 vs 3.0%), & previous aspirin use (24 vs 9%, p<0.05 for all). The 2 groups had otherwise similar baseline clinical & angiographic features. Stent use (29 vs 29%), final TIMI-3 flow (91 vs 92%), mean residual stenosis (22 vs 21%), & cath lab complications (33 vs 29%) were comparable between groups. Patients with prior angina had similar incidence of in-hospital reinfarction (1.3 vs

0.8%), TVR (3.9 vs 2.8%), death (2.2 vs 2.8%), and MACE (6.1 vs 5.7%) as those without prior angina (P=NS for all). Further, during 1-year follow-up, no difference was found in the incidence of death (4.7 vs 5.6%, p=0.60) or MACE (23 vs 17%, p=0.07) between patients with and those without prior angina.

Conclusions: A history of angina prior to acute myocardial infarction does not confer protection from adverse outcomes in patients undergoing primary angioplasty. Our findings challenge the clinical relevance of ischemic pre-conditioning in such patients.

POSTER SESSION

1101 Risk Assessment and Management of Acute Coronary Syndromes: Insights From Large Databases

Monday, March 18, 2002, Noon-2:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1101-33 Characteristics and Outcome of Patients With ST Elevation Versus Non-ST Elevation Myocardial Infarction: Results of the MONICA Augsburg Myocardial Infarction Registry 1985-1995

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Background: The classification of myocardial infarction (MI) has been more and more moved from discerning Q-wave from Non-Q-wave MI to classifying MI by ST- wave dynamics. Data about patient (pat.) characteristics and prognosis in relation to their ST-wave dynamics are scarce. Methods and Results: We, therefore, analyzed ECG-data (Minnesota-Coding) from the MONICA Augsburg Myocardial Infarction-Registry from 1985-1995 (n= 2896; aged 25-75 years; 74% men). ST-Elevation MI (ST-E) was most frequent (59%), followed by MI with unspecific ST-changes (neither elevation nor depression; ST-U; 25%) and MI with ST-depression (ST-D; 16%). Pat. with ST-D were more often diabetics than pat. with ST-E or ST-U (28.1 vs. 21.9 and 20.5%; respectively), were more often female (31.5 vs. 26.3 and 19.7%), had more often a history of angina (47.3 vs. 36.7 and 40.0%) and previous MI (27.6 vs. 19.5 and 23.9%), and were less often treated by thrombolytics (13.6 vs. 38.8 and 12.4%; p for all comparisons < 0.001). In addition, pat. with ST-D were significantly older, had a higher mean pulse rate during admission, and a lower peak CK level than pat. with ST-E (p <0.01 respectively). The 28-day-case fatality-rate was 13.2% for ST-D, 10.8% for ST-E, and 7.5% for ST-U, respectively (significance only for ST-E vs. ST-U; p < 0.001; for ST-E vs. ST-D p > 1). These case-fatality differences were not altered substantially by multivariate testing in a logistic regression model including the above mentioned differences in history and therapy.
Conclusion: 25% of MI-pat. had a non-diagnostic ECG. This group has the lowest mortality. Despite significant differences in presentation and cardiovascular risk-factor history, pat. with ST-elevation did not differ in terms of short-term prognosis from pat. with ST-depression.

1101-34 Opportunities for Enhancing the Use of Evidence-Based Medicines for Acute Coronary Syndromes: Insights From the SYMPHONY Studies

Judith Kramer, L. Kristin Newby, John Simes, Frans Van de Werf, Christopher Granger, Kerry Lee, Manjushri Bhapkar, Robert Califf, Paul W. Armstrong, *University of Alberta, Edmonton, Alberta, Canada, Duke Clinical Research Institute, Durham, North Carolina.*

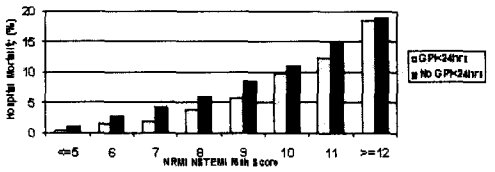
The extent to which evidence-based therapy [Class IA or IB evidence (AHA/ACC 9/2000 and ESC 9/2000)] is applied internationally to the broad cross-section of patients early after acute coronary syndromes (ACS) is unknown. Accordingly, we evaluated this issue in 15,904 patients from 36 countries entered into the Symphony and 2nd Symphony studies of sibrafiban between Aug 1997 and Aug 1999. We analyzed by geographic region the use of concomitant medications between each patient's qualifying ACS event and start of study treatment (median 91 hrs); and to what extent international variations in treatment could be explained by differences in patient risk profile. The data are shown in the Table.
There were important variations in evidence-based treatment of ACS across geographic region, which remained highly significant (p<0.001) after adjustment for all major patient risk factors for future coronary events. Given the greater use of some treatments but lesser use of others within the same region, we believe these findings are unlikely to be driven by cost alone. Our data also indicate substantial global opportunities for improving secondary prevention. Hence continued monitoring of these international patterns of care and development of appropriate interventions to increase adherence to evidence-based guidelines is a desirable next step.

Med Class	Asia	L.America	E.Europe	W.Europe	USA	Canada	Au/NZ
	n=551	n=557	n=2661	n=3431	n=7185	n=871	n=648
ASA	87%	86%	75%	82%	85%	88%	91%
Beta blockers	68%	75%	70%	69%	73%	78%	75%
Lipid lowering	37%	17%	10%	30%	40%	29%	42%
ACE inhibitors	56%	50%	48%	30%	33%	36%	33%
Heparin	37%	61%	55%	52%	78%	79%	51%
LMWH	27%	16%	28%	34%	10%	11%	34%

1101-35 Early Use of Glycoprotein 2b3a Inhibitors and Outcomes in Non-ST Elevation MI: Observations From the NRMI-4

Eric D. Peterson, John G. Canto, Charles V. Pollack, Lori Parsons, Matt T. Roe, Kathee Littrell, Nathan R. Every, Hal V. Barron, for the NRMI-4 Investigators, *Duke Clinical Research Institute, Durham, North Carolina.*

Background: The recent AHA/ACC ACS Guidelines recommend early use of glycoprotein IIb-IIIa inhibitors (GP 2b3a) in non-ST elevation MI (NSTEMI) patients, yet community adoption has been slow.
Methods: We examined the relationship between "early use" of GP 2b3a within 24hrs of admission and in-hospital mortality in 32,710 NSTEMI patients eligible for GP 2b3a, treated at 1,087 hospitals in the NRMI 4 Registry between July 2000-April 2001.
Results: Overall, 24% of eligible NSTEMI patients were begun on a GP 2b3a in <24hrs. Patients treated with GP 2b3a <24 hrs were younger, more likely male, and had chest pain and ST depression on presentation than those not. Unadjusted in-hospital mortality rate was significantly lower in those treated with GP 2b3a <24hrs than those not treated early (3.2% vs 8.5%, p<0.0001). After adjusting for 13 patient risk factors (NRMI NSTEMI risk model, C-index 0.75), and for hospital size, region, teaching affiliation and cath facilities, patients getting GP 2b3a <24 hrs had 32% lower relative risk for in-hospital mortality (adjusted OR 0.68, 95% CI 0.59-0.79). Adjustment for treatment propensity (to receive GP 2b3a<24 hrs) revealed similar results. The Figure displays mortality rates by GP2b3a use <24hrs according to NRMI risk group.
Conclusion: Early use of GP 2b3a within 24 hrs of admission was associated with lower in-hospital mortality across the NSTEMI risk spectrum. As only 24% of eligible patients received early GP2b3a therapy, there is considerable room for quality improvement.



1101-36 Comparison of Characteristics, Treatment, and Outcomes of Patients Enrolled Versus Not Enrolled in a Clinical Trial: Findings From TIMI 9 Registry and 9B Trial

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Background: Because mortality in clinical trials (CT) is generally lower than in registries of clinical practice, it has been suspected that patients are lower risk. However, little is known about the characteristics of patients included vs. not in CT. **Methods**: To address this issue, TIMI 9 Registry prospectively evaluated characteristics and in-hospital outcomes for ST-elevation MI patients at 20 hospitals during the conduct of TIMI 9B trial.We compared characteristics, treatment and outcomes of patients in TIMI 9B trial (N=3002), with others eligible for thrombolysis but not enrolled in the TIMI 9B trial (N=296), and with those not-eligible for thrombolysis by ACC/AHA criteria at the same centers (N=282). **Results**: At TIMI 9 Registry hospitals, 46% of eligible patients were enrolled in TIMI 9B. Across the three groups, a gradient of both high-risk baseline characteristics, use of reperfusion therapy and mortality was observed. In addition, although we did not assess contraindications for each medication, use of aspirin, (and beta-blockers, ACE inhibitors) both initially and at discharge was lower among eligible/not enrolled patients (p<0.0001 for aspirin) or ineligible patients.(Table)
Conclusion: In this prospective registry, we found that half of eligible patients were enrolled. Those not enrolled had higher risk characteristics and worse outcomes; however, they also were treated less frequently with guideline-recommended medications, which may have contributed to their higher mortality.

	Eligible/ enrolled	Eligible/ not enrolled	Not eligible/ not enrolled	3-way p
Age (years)	60.1 ± 11.9	62.3 ± 13.5	67.5 ± 12.6	<0.0001
Female gender	25.1%	32.4%	39.5%	<0.0001
Aspirin	99.4%	91.5%	75.2%	<0.0001
Thrombolysis	99.6%	59.8%	22.5%	<0.0001
Primary PCI	0	12.5%	12.7%	<0.0001
In hospital death	5.1%	8.4%	19.8%	<0.0001
Death + MI+ Shock+ severe CHF	9.0%	15.9%	30.1%	<0.0001

1101-37 Approach After Thrombolytic Therapy: Invasive Versus Conservative Management: Global Registry of Acute Coronary Events

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Background: Thrombolytics (lytics) reduce mortality of patients (pts) with acute ST segment elevation MI (STE MI). However, the impact of a subsequent invasive strategy on outcomes has not been studied in an international population-based setting.
Methods: 1,766 pts enrolled in GRACE with STE MI who received lytics were divided into